allegation notwithstanding.

Paraphrasing the language of Applicant's generic claim, the instant invention relates to a method of making raw sausage by the steps of proving diminuted raw sausage meat and adding to each kilogram of the sausage meat from about 4 mg to about 25 mg of folic acid or folate. This, as the state of the art relied upon by the Examiner unambiguously reveals, has never been done before. Moreover, contrary to conventional sausage production processes, Applicant's method does not involve, or rely upon, any heat treatment for preservation purposes. The amount of folic acid or folate added, in Applicant's opinion does constitute an invention, not least because it yields technical results nowhere deducible from the state of the art. These technical results or effects, as will be set forth *infra* also could not have been predicted and, accordingly, practicing the invention to attain these results or effects and quality, for that matter, was totally unobvious to any person skilled in the art.

More specifically, and to contravene the Examiner's argument, adding folic acid or folate to raw sausage dough has nothing to do with the desirability of adding folic acid or folate to food cereals as a means of reducing the risk of pregnancy affected by a neural tube birth defect or vascular disease, as taught by Radar. Rather, adding these substances in the defined amounts to raw sausage meat, results in improved and accelerated ripening of the final product, and, during such ripening, in an enzymatic fermentation which, in turn, preserves the sausage. No such considerations enter into the reasoning for adding folic acid or folate to food cereals. Unlike raw sausage meat pressed into casings, cereals want neither ripening nor preservation. Among other things, the fermentation results in micro organisms converting sugar present in the sausage to lactic acid, and this is one reason for sausage made in accordance with Applicant's invention not being as perishable as has heretofore been the rule.

Applicant has pointed out in his amendment of 14 November 2008, that part of the folic acid or folate is consumed by metabolistic processes of micro organisms. Tests conducted by Applicant have confirmed that this process

contributes significantly to the preservation of the sausage. Nothing in the state of the art suggests, much less discloses, anything even remotely similar. This, in Applicant's view, constitutes a preponderance of evidence to the effect that his invention is new as well as unobvious.

Owing to metabolistic processes in the yet unripened sausage dough, a reduction in the folic acid or folate may, of course be expected. The exact reduction is a function of biological, chemical and physical parameters; but as tests conducted by Applicant have shown the terminal amount of folic acid or folate in the fully ripened sausage stands in no linear relation to the amount of folic acid or folate added to the initial raw sausage dough. These parameters defy being brought into tune, as it were, with each other during sausage production. It is thus possible that under one given set-up the concentration of folic acid or folate may be reduced more quickly than under another set-up. Obviously, the ripening processes differ correspondingly.

The parameters which chiefly determine, or at least contribute to, the ripening process of the sausage are the pH value of the sausage dough, the kind and quantity of the micro organism starter cultures, e.g. bacterial and fungous cultures, temperature or the change of temperature over time during the ripening process of the sausage, quantity of light absorbed, the quantity of carbohydrates in the sausage, humidity, as well as a large number of further biological, chemical and physical factors which may affect the reduction of folic acid or folate during the ripening process to a greater or lesser degree.

This, too, indicates that Applicant's process is patentable. For a person skilled in the art, even if he were to add folic acid or folate, would have no way of knowing how much folic acid or folate would remain in the sausage once the production process has terminated, i.e. after ripening. Thus, it is respectfully submitted that the Examiner's arguments in the current Office Action are missing the point, since adding folic acid or folate to the sausage dough gives no indication of how much of these substances will remain in the sausage following its ripening. The mere adding, as proposed by the Examiner, does not suffice to

make intelligent statements about the resulting sausage, such as whether the remaining folic acid or folate available to the consumer in the ripened raw sausage is healthful or neutral. Thus, adding but small quantities may result in raw sausage devoid of any folic acid or folate, whereas the addition of excessively large quantities may result in saturation.

As regards any optimum quantity of folic acid or folate added under the conditions referred to *supra,* Applicant has subjected raw sausage to a number of tests. The enclosed diagram depicts the results of a series of performed tests. More specifically, the diagram depicts the chronological progress of folic acid concentration in the ripening process during raw sausage production after an initial addition of 20 mg/kg of folic acid to the raw sausage dough. Several individual sausages were prepared which, following a predetermined ripening time, were analytically examined for their folic acid content.

As may be seen from the enclosed diagram, even after a single day and within certain error limits the folic acid concentration was reduced. After about 10 to 15 days the folic acid concentration had become stabilized at a value of from about 8 to about 9 mg/kg. During the continuing ripening process, which for purposes of the tests was carried on for a total of 50 days, this value of concentration did not substantially change. It is to be noted, that the error statements in the diagram are the result of an analytic determination of the folic acid which is more difficult for raw sausage of a lesser degree of ripening and, therefore, leads to greater errors.

It is also to be noted that as shown in the diagram, the change over time of the folic acid concentration will become typical without necessarily equaling an exponential reduction. Nevertheless it can be determined that under different starting conditions the progress over time of folic acid concentration during the ripening process qualitatively substantially equals the shown progress, with saturation being reached at different points in time and at different values of concentration. In this context, the saturation values are a function of the initially added quantity of folic acid or folate. Furthermore, the saturation is a function of

the termination of the ripening process. It is urged that this, too, is an indication of the invention being patentable.

It may thus be said that the addition of folic acid or folate in raw sausage production yields a number of technical and unexpected effects which no skilled artisan would have been able to recognize, much less predict, without first conducting tests of the kind conducted by the Applicant. Furthermore, within the limits of the experimental characterization of the ripening process a number of further technical effects during the ripening process may be determined following the adding of folic acid or folate. Among these are the accelerated reduction of the pH value, a more rapid reddening, improved development of aroma, a reduction of added starter cultures as well as a general acceleration of the ripening process. These effects are neither suggested, much less disclosed, by the state of the art of record nor would they have been obvious to a person skilled in the art.

Of course, Applicant is aware of the fact that adding folic acid or folate to raw sausage may constitute an improved, perhaps even elegant, manner of making these substances available to a consumer. While the Examiner has commented extensively on the health-promoting qualities of these substances, she seems in her arguments to have overlooked that the addition of folic acid or folate to food for purposes of preventing diseases of the kind referred to, would, in the context of sausage, make sense only if following ripening of the sausage sufficient quantities of these substances remain. Particularly in cases where only very small quantities are added to the initial sausage dough may it be assumed that they will be metabolized completely during the ripening process.

It will now be apparent that the quantity of folic acid or folate remaining in the ripened sausage must be neither too little nor too much. As a matter of interest, Applicant wishes to point out that while the FDA has recommended a daily dose of 1 mg of folic acid in the consumption of cereal products (see the enclosed fact sheet: "Folic Acid Fortification"), no recommended quantities have been set forth in connection with cold cuts. Nevertheless, a daily dose of from

about .43 to about 1.4 mg is generally recommended.

By adding 4 to 25 mg/kg of folic acid or folate to raw sausage dough Applicant has sought to solve two complex problems in addition to those referred to *supra*. On the one hand has wanted to provide improved ripening of the raw sausage and on the other hand he is at the same time attempting to provide for consumers an inconspicuous source of nutrition-enriching folic acid or folate. The claimed amount of from 4 to 25 mg/kg of folic acid or folate was found optimally to solve these problems.

The use of no more than 4 mg/kg of folic acid or folate has resulted in slight technical advantages in the sense discussed hereinbefore; higher concentrations could, however, be shown to yield less ambiguous and more precisely definable advantages. The use of 15 - 25 mg/kg of folic acid or folate has led to optimum results. Any higher concentrations did not yield additional technical advantages.

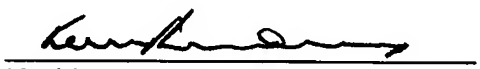
At the same time, Applicant's analyses of the ripened raw sausages prepared with 20 mg/kg of folic acid or folate in their raw sausage dough have revealed an average content of 10 mg/kg (the annexed diagram depicts about 8 mg/kg, a value somewhat below the average) of folic acid or folate. At a daily consumption of 40 g of the sausage this equals about 400 µg of folic acid or folate. This, of course, corresponds to the lower daily dose of folic acid or folate recommended by the FDA (see enclosed fact sheet "Folic Acid Fortification"). The tests also proved that when 15 mg/kg of folic acid or folate are used, only 6 mg/kg remains following ripening of the raw sausage. This, at a daily ration of 40 g of sausage, amounts to 60% (based on a daily dose of 400 µg of folic acid or folate) of the daily minimum requirement. Furthermore, it was found that using 10 mg/kg of folic acid or folate leaves only 2.5 mg which, again based on a daily raw sausage ration of 40 g, satisfies 25% of the daily minimum requirement. In this connection, it is to be noted that as stated *supra* the amount of folic acid or folate remaining in the raw sausage does not decrease linearly relative to the quantity of folic acid or folate added to the initial sausage dough. It is earnestly

quantity of folic acid or folate added to the initial sausage dough. It is earnestly urged, that this, too, is an indication of the patentability of the invention disclosed by Applicant.

The various subclaims objected to by the Examiner on grounds of obviousness all depend from, and add elements considered advantageous to, the generic and, as has been pointed out above, unobvious claim.

Applicant earnestly urges that in light of his above arguments his invention is unobviousness, not least because the prior art cannot arguably be said to teach anything to a person skilled in the art which would lead him without extensive experimentation to Applicant's invention. Reversal of the current rejection of the claims is, therefore, indicated and allowance of the application courteously requested.

Respectfully submitted,



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Enclosures

**U. S. Food and Drug Administration**
**Office of Public Affairs**
**Fact Sheet**
**February 29, 1996**

# FOLIC ACID FORTIFICATION

(See updated information on folic acid, FDA Consumer, February 1999)

## Background:

The U.S. Public Health Service recommended in September 1992 that all women of childbearing age consume 400 micrograms (ug) of folic acid daily to reduce their risk of having a pregnancy affected with spina bifida or other neural tube defects. Folic acid is a B vitamin. For women, this amount of folic acid on a daily basis spina bifida or anencephaly, both of which are neural tube defects (NTDs) in the baby.

PHS suggested several approaches by which this level could be reached:

- Improved dietary habits
- Fortification of the U.S. food supply
- Daily use of folic acid supplements by women throughout their childbearing years.

## FDA Action:

In keeping with the recommendations of PHS and the FDA Food Advisory Committee called to study these issues, the Food and Drug Administration is requiring that folic acid be added to specific flour, breads and other grains. These foods were chosen for fortification with folate because they are staple products for most of the U.S. population, and because they have a long history of being successful vehicles for improving nutrition to reduce the risk of classic nutrient deficiency diseases.

These fortified foods include most enriched breads, flours, corn meals, rice, noodles, macaroni and other grain products.

**Under the terms of the new rule:**

- Fortification levels will range from 0.43 milligrams to 1.4 mg per pound of product.
- Fortification of grain products at these levels will allow the daily intake from all sources to remain below the recommended upper limit of 1 mg per day.
- The amount of folic acid that will be consumed through foods fortified at these levels is considered safe for all population (age/gender) groups.
- Manufacturers will be allowed to make claims on the labels that the fortified products contain folic acid and that adequate intake of the nutrient may reduce the risk of neural tube defects.

FDA also emphasizes that adequate levels of folic acid, in the form of folate, can be obtained by eating natural sources such as:

- Leafy dark green vegetables
- Legumes (dried beans and peas)
- Citrus fruits and juices
- Most berries

In addition, women can assure adequate intake by taking dietary supplements containing folic acid.

The new rule takes account of the finding in PHS' recommendation that total folate consumption should be kept under 1 mg per day. This is because higher intake may complicate the diagnosis of pernicious anemia, one form of vitamin B12 deficiency, which especially affects older people.

## Neural Tube Defects:

Neural tube defects, including spina bifida and anencephaly, are a common birth defect.

- Approximately 2,500 infants are born each year in the U.S. with an NTD. About half this number are though to be related to inadequate folate intake by the mother. Other NTDs have different causes that are not well understood.
- Spina bifida is a condition in which the spinal cord is exposed. A majority of babies born with spina bifida grow to adulthood with varying degrees of disability, ranging to problems with bowel and bladder control, and paralysis. Many may require a series of operations and other treatments.
- In anencephaly, infants die shortly after birth because most or all of the brain is absent.

Since NTDs develop very early in pregnancy (18-30 days after conception), often before a woman knows she is pregnant, it is essential that adequate intake of folic acid be maintained throughout the childbearing years.

Women who have had a prior NTD-affected pregnancy are at high risk of having a subsequent affected pregnancy. When these women are planning to become pregnant, they should consult their physicians for advice.

## Pernicious Anemia & Recommended Daily Limit:

Because the effects of high intakes of folic acid are not well known, but do include complicating the diagnosis of vitamin B12 deficiency, care should be taken to keep total folate consumption under 1 mg per day, except under the supervision of a physician.

- About 10 to 20 percent of the elderly are diagnosed as having low vitamin B12 levels.
- The effects of folic acid at levels between 1 and 5 mg are not well known, but include complicating the diagnosis of vitamin B12 deficiency.
- Among persons with pernicious anemia, one form of vitamin B12 deficiency, adverse effects have been reported with daily intakes of 5 mg folic acid and above.
- Because FDA has a mandate to set fortification levels that are safe for all population groups, lack of long term data makes it impossible to conclude that continuous intakes of 1 mg or more daily would be safe.

The FDA rule is designed to keep total folic acid intake under the 1 mg level.

**History of Food Fortification:**

Addition of iodine to salt was one of the earliest successful fortification programs. Iodine fortification was initiated in the U.S. in 1924 to prevent goiter, cretinism and other symptoms of severe iodine deficiency.

In the early 1930s, vitamin D was first added to cow's milk to aid in absorption of calcium and phosphorus, preventing development of rickets.

In 1938, voluntary enrichment of flours and breads was initiated to prevent the development of deficiency diseases in the general population. Enrichments included thiamin for beriberi, niacin for pellagra, riboflavin essential for proper functioning of vitamin B6 and niacin, and iron for iron deficiency anemia. Mandatory requirements were effective in 1943.

There are various other fortification requirements to enhance the quality of food such as vitamin A added to low and nonfat cow's milk and certain other dairy products, and lysine added to certain corn products to enhance protein quality.

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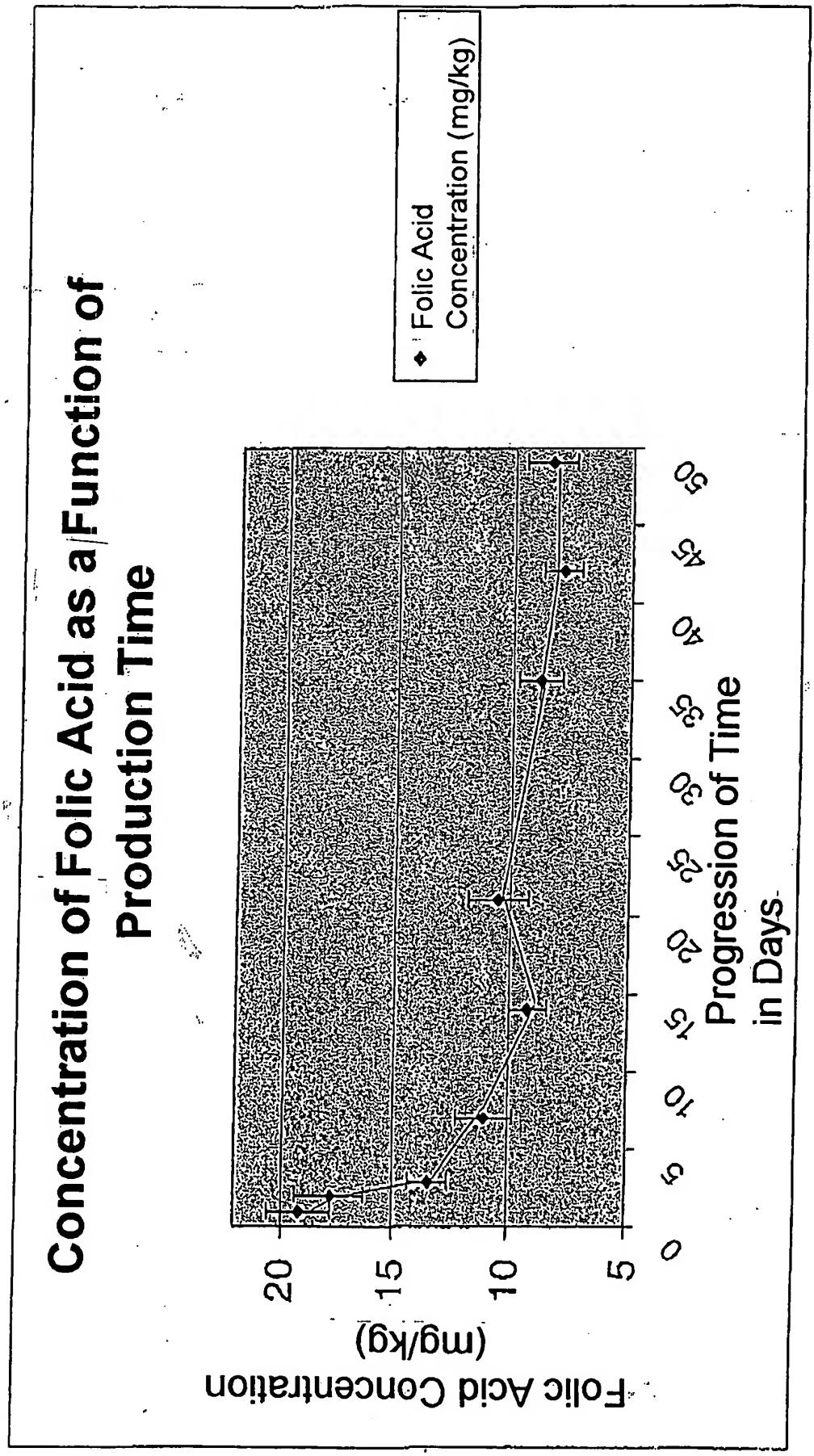
The 1994 FDA Consumer magazine article reprinted below provides additional information on folic acid and neural tube defects.


Concentration of Folic Acid as a Function of Production Time
Folic Acid Concentration (mg/kg)
Folic Acid Concentration (mg/kg)
20
15
10
5
0
5
10
15
20
25
30
35
40
45
50
Progression of Time in Days